

09/857843

CLAIMS 531 Rec'd PC

11 JUN 2001

What we claim is:

1. An immunogenic composition for conferring protection in a host against disease caused by *Haemophilus influenzae*, comprising:

at least two different antigens of *Haemophilus influenzae*, at least one of which antigens is an adhesin and the other of which antigens is not an adhesin.

2. The immunogenic composition of claim 1 wherein said antigen which is an adhesin is a high molecular weight (HMW) protein of a non-typeable strain of *Haemophilus influenzae*.

3. The immunogenic composition of claim 2 wherein said HMW protein is a HMW1 or HMW2 protein of the non-typeable strain of *Haemophilus influenzae*.

4. The immunogenic composition of claim 1 wherein the antigen of *Haemophilus influenzae* which is not an adhesin is a non-proteolytic heat shock protein of a strain of *Haemophilus influenzae*.

5. The immunogenic composition of claim 4 wherein the non-proteolytic heat shock protein of a strain of *Haemophilus influenzae* is an analog of *Haemophilus influenzae* Hin47 protein having a decreased protease activity which is less than about 10% of that of natural Hin47 protein.

6. An immunogenic composition for conferring protection in a host against disease caused by *Haemophilus influenzae*, which comprises:

an analog of *Haemophilus influenzae* Hin47 protein having a decreased protease activity which is less than about 10% of that of natural Hin47 protein, and

a high molecular weight (HMW) protein of a strain of non-typeable *Haemophilus influenzae*.

7. The composition of claim 6 wherein said HMW protein is present in said composition in an amount which enhances the immune response in the host to the Hin47 protein.

8. The composition of claim 7 wherein said HMW protein is present in the said amount while the individual immunogenicities of the proteins in the composition is not impaired.

09857843-091701

9. The composition of claim 6 wherein said analog of Hin47 protein is one in which at least one amino acid of the natural Hin47 protein contributing to protease activity has been deleted or replaced by a different amino acid and which has substantially the same immunogenic properties as natural Hin47 protein.
10. The composition of claim 9 wherein said at least one amino acid is selected from the group consisting of amino acids 91, 121 and 195 to 201 of natural Hin47 protein.
11. The composition of claim 10 wherein Serine-197 is replaced by alanine.
12. The composition of claim 10 wherein Histidine-91 is replaced by alanine, lysine or arginine.
13. The composition of claim 12 wherein Histidine-91 is replaced alanine.
14. The composition of claim 10 wherein Asp-121 is replaced by alanine.
15. The composition of claim 8 wherein said HMW protein is an HMW1 or HMW2 protein of a non-typeable strain of *Haemophilus influenzae*.
16. The composition of claim 15 wherein the HMW1 and HMW2 proteins are produced recombinantly.
17. The composition of claim 15 wherein said HMW1 and HMW2 proteins are derived from the respective strain of non-typeable *Haemophilus influenzae* and possess respective molecular weights as set forth in the following Table:

Molecular Weight(kDa)	Non-typeable <i>H. influenzae</i> Strain					
	12	JoyC	K21	LCDC2	PMH1	15
Mature Protein: HMW1	125	125.9	104.4	114.0	102.4	103.5
HMW2	120	100.9		111.7	103.9	121.9

18. The composition of claim 6 further comprising an adjuvant.
19. The composition of claim 18 wherein said adjuvant is aluminum hydroxide or aluminum phosphate.
20. The composition of claim 6 comprising
about 25 to about 100 μ g of the Hin47 protein analog, and
about 25 to about 100 μ g of the HMW protein.
21. The composition of claim 6 further comprising at least one additional antigenic component for conferring protection against infection caused by another pathogen.

22. The composition of claim 21 wherein said at least one additional antigenic component is selected from the group consisting of diphtheria toxoid, tetanus toxoid, pertussis antigens, non-virulent poliovirus and PRP-T.
23. The composition of claim 22 wherein said pertussis antigens are selected from the group consisting of pertussis toxoid, filamentous hemagglutinin, pertactin and agglutinogens.
24. The immunogenic composition of claim 1 or 6 when used as a vaccine.
25. A method of immunizing a host against disease caused by infection with *Haemophilus influenzae*, including otitis media, which comprises administering to the host an immunoeffective amount of a composition as claimed in claim 1 or 6.
26. The use of at least two different antigens of *Haemophilus influenzae*, at least one of which is an adhesin, in the manufacture of a vaccine for conferring protection against disease caused by infection with *Haemophilus influenzae*, including otitis media.

09657843-094704